REMARKS

The only issues outstanding in the Office Action mailed December 27, 2006, are the requirement for restriction and the rejections under 35 U.S.C. §112 and §102. Reconsideration of these issues, in view of the following discussion, is respectfully requested.

Requirement for Restriction

The requirement for restriction is again traversed, for the reasons of record. Applicants will take appropriate action such time as allowable subject matter is indicated. Moreover, rejoinder under appropriate circumstances is urged.

Rejections under 35 U.S.C. §102

The rejection of claim 33 under 35 U.S.C. §102(b) is rendered mute by cancellation of the claim.

Rejections under 35 U.S.C. §112

Claims 22 and 23 have been rejected under 35 U.S.C. §112, second paragraph. Reconsideration of this rejection is respectfully requested.

The office action objects to the term "additional pharmaceutically active compound" which appears in these two claims. Although it is argued in the office action that such materials are not defined in the specification, in fact, "other known therapeutic agents" administered along with the compounds of the invention are listed in considerable detail at pages 30 – 33. Moreover, one of ordinary skill in the art would understand that "additional pharmaceutically active compounds" is intended to refer to any such materials which have therapeutic pharmaceutical effect. Since the office action does not allege that applicants intend to *exclude* any pharmaceutically active compound, it is not seen that the term is indefinite. Accordingly, withdrawal under 35 U.S.C. §112 is respectfully requested.

Claims 1-7, 22-23, 28-29, and 31-34 have been rejected under 35 U.S.C. §112, first paragraph. It is argued, at page 4 of the specification, that while various compounds are enabled, the specification does not "reasonably provide enablement for all the thousands of molecules encompassed by the generic formulae I-VII." Applicants respectfully disagree with this analysis. The heart of this rejection, as stated at page 6 of the office action, appears to be based on the breath of present claims, in the argument that "formula I-VII" encompass a "plethora" of functional groups. At the outset, it is noted that compounds of formulas II-VII are *intermediates*, and thus their utility is to make compounds of formula I. *In re Lalu*, 223 U.S.P.Q. 1257 (Fed. Cir. 1984). Since compounds of formula I have utility, as discussed below, compounds of formula II-VII satisfy §112.

The specification teaches that the compounds of formula I regulate tyrosine kinase signal transduction, and this statement is supported with a discussion of the methods used to determine TIE-2 activity in the subject compounds, see pages 38-39 of the Specification. It is further taught that the compounds thus are useful to treat solid tumors, cerebral tumors, tumors of the genito-urinary tract, tumors of the lymphatic system, stomach tumors, laryngeal tumors, lung tumors, monocytic leukaemia, lung adenocarcinoma, small cell lung carcinoma, pancreatic cancer, glioblastoma or breast carcioma. Clearly, this discussion, *without more*, is sufficient to establish utility of the application for purposes of §112 of the statute, as it constitutes a scientifically supportable statement of utility which would be plausible to one of ordinary skill in the art.

It is well established that an unsupported suggestion that reactants within a class defined by claims in a typical method of use application would not work, or that such claims embrace inoperative members, is insufficient basis alone for rejecting the claims. See *Ex parte Janin*, 209 U.S.P.Q. 761 (POBA 1979). In fact, it is clear that recitations in an Applicants' specification *must* be taken by the PTO as an assertion that all compounds encompassed in the claims are operative in the invention, in the absence of reasons or evidence to the contrary. *In re Marzocchi*, 439 F.2d 220, 169 U.S.P.Q. 367 (CCPA 1971).

The first paragraph of 35 U.S.C §112 requires only *objective* enablement. Where a specification teaches the manner and process of making and using the invention, the specification *must* be taken as sufficient under §112, unless there is reason to doubt the truth of these statements. See *Marzocchi, supra*. Applicants' specification clearly enables one to make and use the disclosed compounds in the claimed methods, as evidenced from the disclosure containing

pharmaceutical formulations and dosages and the examples which also detail the production of a pharmaceutical formulations.

On the one hand, it is submitted that the Examiner has not provided any such reasons or evidence to doubt the assertion of utility in the specification other than the breadth of the claims, and, thus, the further steps of the analysis as set forth in *Marzocchi* e.g., the discussion of *In re Wands* in the office action, are not reached. The breadth of the claims does not rise to the level of such reasons or evidence. As clearly stated in *Marzocchi*, mere *breadth* of the claims does not, without more, result in non-enablement:

> Turning specifically to the objections noted by the Board as indicated above, it appears that these comments indicate nothing more than a concern over the *breadth* of the disputed term. If we are correct, then the relevance of this concern escapes us. It has never been contended that Applicants, when they included the disputed terms in their specification, intended only to indicate a single compound. Accepting, therefore, that the term is a generic one, its recitation must be taken as an assertion by Applicants that all of the 'considerable number of compounds' which are included in the generic term would, as a class, be operative to produce the asserted enhancement of adhesion characteristics. The only relevant concern of the patent office under these circumstances should be over the *truth* of any such assertion. The first paragraph of §112 requires nothing more than *objective enablement.* How such a teaching is set forth, either by the use of illustrative examples or by broad term analogy, it is of no importance.

Marzocchi, *supra*. (Emphasis in original.) Thus, the concern expressed in the Office Action, apparently that the compounds used in the claimed methods are broadly defined, does not provide the reasons or evidence necessary by *Marzocchi* to pass beyond the necessity merely for objective enablement.

Further, in this regard, it is important to note, as a matter of law, that it is not necessary for Applicants' *method* claims to exclude inoperative embodiments, inasmuch as the claims are interpreted in light of the level of understanding one of ordinary skill in the art and, for methods, are interpreted to be *per se* functional. See *In re Angstadt*, 190 U.S.P.Q. 214 (CCPA 1976) and *In re Dinh-Nguyen*, 181 U.S.P.Q. 46 (CCPA 1974). These cases state that, for method claims, inoperative embodiments are not encompassed therein and the only

question is whether it would be undue experimentation for one of ordinary skill in the art to determine the scope of the claim. This issue is discussed more fully below. Moreover, anti-tumor utilities are no longer to be considered to be "special", i.e., per se incredulous, by the Patent and Trademark Office. See *Ex parte Rubin*, 5 U.S.P.Q. 2d 1461 (BPAI 1987). As such, applications claiming these methods are, therefore, no more than typical method of use applications wherein the existence of reliable screening protocols correlatable with pharmaceutical activity in humans is sufficient to satisfy §112, in the absence of reasons to the contrary. As noted above, screening protocols for determining the efficacy of the compounds in the anti-tumor utilities are set forth in the specification, and, the details of using a given compound can be determined by routine testing using a known protocol which is correlated with human activity. The PTO has not alleged it would have been undue experimentation to determine the *scope* of the present method claims. It is important to note that a determination of undue experimentation must be considered on a *compound by compound* basis. The mere fact that a claim is broad does *not* mean that it is undue experimentation is required to determine enablement of the compounds therein, if it is not undue experimentation to determine enablement for *each* compound in the scope of the claim. See, for example, *In re Colianni*, 195 U.S.P.Q. 150 (CCPA 1977). One of ordinary skill in the art can easily determine, with the protocols given in the specification, whether a given compound has the utility stated. Thus, the mere fact that many compounds must be tested is not dispositive of lack of utility.

Moreover, applicants respectfully disagree with the analysis in the office action that one of ordinary skill in the art would be unable to prepare the various compounds of the invention. On the one hand, objective enablement is present, as beyond an assertion of divergence of the various compounds claimed, no reasons or evidence are given why one of ordinary skill in the art would not be able to prepare a given compound. Moreover, an exhaustive description of how to make and use the compounds of the invention, beyond the focus of the office action on just the examples, is present in the specification. For example, pages 15-25 contain an exhaustive description of how to make the compounds, including how to separate them. Such preparation is but routine chemistry to one of ordinary skill in the art.

It is thus respectfully submitted that one of ordinary skill in the art can make and use the present application, without undue experimentation, and moreover, that reasons or evidence to doubt the objective enablement present in the specification have not been

adequately provided. According, under the rationale of *In re Marzocchi, supra*, it is clear that the application fully satisfies the requirements of 35 U.S.C. §112, and withdrawal of the rejection is respectfully requested.

The claims in the application are submitted to be in condition for allowance. However, should the examiner have questions or comments, he or she is cordially invited to telephone the undersigned at the number below.

Respectfully submitted,

_____

Harry B. Shubin, Reg. No. 32,004
Attorney/Agent for Applicant(s)

MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

Attorney Docket No.: MERCK-2808
Date: March 27, 2007

HBS/cak